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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,568	09/15/2003	Steven Z. Wu	50623.335	2840

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EXAMINER	
SHEIKH, HUMERA N	
ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/663,568	WU ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25 and 27-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25 and 27-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Amendment and Response after Non-Final Office Action and Applicant's Arguments/Remarks, all filed 02/20/08 is acknowledged.

Applicant has overcome the following rejection by virtue of the amendment and/or persuasive remarks: (1) The 35 U.S.C. §102(e) rejection of claims 25, 28-30 and 32 over Golomb (U.S. Pat. No. 6,719,998) has been withdrawn.

Claims 25 and 27-32 are pending in this action. Claims 25 and 32 have been amended. Claims 26 and 33 have been cancelled herein. Claims 1-24 have previously been cancelled. Claims 25 and 27-32 remain rejected.

* * * * *

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 25 and 28-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Golomb *et al.* (hereafter "Golomb") (U.S. Pat. No. 6,719,998).

Golomb *et al.* ('998) teach compositions and methods for the treatment of restenosis (see Abstract); (col. 1, lines 7-10); (col. 7, lines 4-14). The method of treatment of restenosis comprises administering an effective amount of active ingredient (biphosphonates – (BP) or pyrophosphate), a complex thereof or a pharmaceutically acceptable salt or ester thereof (col. 2, lines 33-67).

The invention provides for the treatment of in-stent restenosis (col. 3, lines 35-50). Golomb *et al.* teach that the active ingredient may be formulated in a manner allowing its incorporation onto the stent, which will yield administration of said active ingredient directly at the site. The active ingredient may be formulated in that manner, for example, by including it within a coating of the stent. Examples of coating are polymer coatings, e.g., made of polyurethane or a gel (col. 3, lines 47-60).

The compositions may be prepared in various forms such as capsules, tablets, aerosols, solutions, suspensions, or as a coating of a medical device such as a stent (col. 3, line 64 – col. 4, line 9).

In a preferred embodiment of the invention, the active ingredient is formulated into a particulate form. This may be achieved by encapsulating or impregnating the active ingredient into particles, e.g., polymeric particles, lipid vesicles or liposomes (col. 4, lines 9-13). Furthermore, such particles may be particles of polymerized active ingredient (col. 4, lines 13-23).

At column 5, lines 55-58, it is taught that pyrophosphate is preferably formulated and administered in a liposome or a polymeric particle preparation.

The composition of the invention may comprise active ingredient either in their free acid form, complexed with metal cations or may be in the form of salts or esters or they may be polymerized to yield polymers of up to 40 monomers. The salts or polymers may be in a micronized particulate form having a diameter within the range of about 0.01-10 μm (col. 5, line 58 – col. 6, line 4). (This meets Applicant's claimed range of particles of 0.5 to 2 microns – instant claim 29).

Golomb *et al.* teach that the active ingredient may be encapsulated or embedded in inert polymeric particles such as, for example, any of the microcapsules, nanocapsules, nanoparticles, nanospheres, microspheres, microparticles, etc. known in the art. The release of the active ingredient from such particles may be a controlled release, which can result in prolonged and enhanced effect and uptake of the active ingredient (col. 6, lines 18-24.

Pharmaceutical carriers or diluents are disclosed at col. 6, lines 25-37). The composition used for injection may be selected from emulsions, solutions, suspensions, colloidal solutions containing suitable additives, etc. (col. 6, lines 38-40).

The compositions may be administered by any route, which effectively transports the active compound to the appropriate or desirable site of action. Modes of administration include intravenous, intra-arterial and intramuscularly. Local administration can be carried out by means of a suitable oozing/sweating balloon known in the art (col. 6, lines 41-50).

The compositions may be administered by perivascular delivery by coating of the delivery system on a balloon or stent (col. 6, lines 51-62).

The instant invention is drawn to a drug loaded stent comprising a coating layer disposed on the stent body and having polymeric particles containing a drug embedded within the coating layer. It is the position of the Examiner that the instant stent being claimed by Applicant would be *prima facie* obvious given the teachings of Golomb. Golomb explicitly teaches methods and compositions for treating restenosis comprising application of a coating layer onto medical devices, such as stents, whereby the coating layer is comprised of polymeric particles and active substance(s). Golomb teaches that their methods and compositions are effective for treating in-stent restenosis, using stent devices, as similarly claimed herein by Applicant. Thus, the methods

and compositions for treating restenosis by application of coating materials onto stent devices as taught by Golomb meets Applicant's instant claims, since the compositions of Golomb are suitable for their intended use; namely for application of drug-loaded coating compositions onto medical devices, particularly stents.

Hence, the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, given the teachings of Golomb *et al.*

* * * * *

Claims 27, 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Golomb *et al.* (hereafter "Golomb") (U.S. Pat. No. 6,719,998) as applied to claims 25 and 28-30 above and further in view of Wang (U.S. Pat. No. 6,379,379).

The teachings of Golomb are discussed above. Golomb do not teach radiochemicals (radioactive isotopes) and do not teach that their coating layer is *free from* any therapeutic substances.

Wang ('379) teaches a stent that includes a polymeric coating or coating(s) on one or both end portions of the stent (see Abstract); (col. 1, line 10 - col. 3, line 17). The coating may be used as a drug delivery system to treat restenosis, whereby the drugs include radiochemicals to irradiate and prohibit tissue growth (col. 5, lines 32-46). Wang teaches that the stent can have multiple layers of different polymers with the same or different drugs. For example, the stent

can have two layers of the same polymer coating (18) with one layer with drug and another layer *without* drugs (col. 6, lines 24-30); (col. 4, lines 46-64).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate radioactive chemicals and coatings that are free of active substance, as taught by Wang within the methods and compositions taught by Golomb. One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Wang explicitly teaches that the stents include drugs, such as include radiochemicals, effective for irradiation and prohibition of tissue growth. Wang further teaches that the stents can have multiple layers of the same polymer coating, whereby one layer has drug incorporated into it, while the other layer is devoid of drug(s), thus providing different polymer coating layers and materials. The expected result would be an enhanced stent for the beneficial treatment of restenosis.

* * * * *

Pertinent Art

Prior Art made of record, deemed relevant and cited of interest by the Examiner:

- Alt (U.S. Pat. No. 5,871,437) (02/1999):

  Alt teaches a radioactive stent for treating blood vessels to prevent restenosis. The stent is coated with biodegradable and non-biodegradable polymer coatings (see Abstract and column 6, lines 12-39).

Response to Arguments

Applicant's arguments filed 02/20/08 have been fully considered and were found to be partially persuasive.

- **Rejection under 35 U.S.C. §102(e) over Golomb (U.S. Pat. No. 6,719,998):**

Applicant's arguments with regards to the §102(e) rejection have been considered and were found persuasive, by virtue of the amendment to the claims. Accordingly, the §102(e) rejection has been withdrawn.

- **Rejection under 35 U.S.C. §103(a) over Golomb (U.S. Pat. No. 6,719,998):**

Applicant argued, "With respect to claim 25, nowhere does Golomb disclose, either expressly or inherently, drug-containing polymeric particles embedded within a coating layer on a stent."

Applicant's arguments have been considered but were not persuasive. Golomb explicitly teaches compositions comprising active ingredient that is formulated in a manner to allow it's incorporation onto a stent, such as for example, *by including it within a coating of the stent*. See column 3, lines 55-60. This teaching vividly suggests that the active ingredient is an intimate part of the coating layer and thus, clearly reads on Applicant's claimed limitation of "polymeric particles embedded within a coating layer".

Applicant argued, "In addition, nowhere does Golomb disclose, either expressly or inherently, that the coating layer includes an additional "...polymer different than the polymer from which the particles are made".

This argument was not deemed persuasive with regards to the obviousness rejection. Applicant has not established any unexpected or superior results, which accrues from the use of providing an additional polymer other than the particles from which the polymer is made. The prior art provides for a composition having essentially the same elements, being used in the same art area, to achieve the same results and treat the same problems, the Applicant providing no showing of any unexpected result. Furthermore, the argument that "the present invention includes a polymeric material, i.e., polymeric particle, inside of another polymeric material..." was not persuasive since Applicant's arguments do not establish the scope of claims presented. The claims as presently recited do not require that the polymeric particle be inside of another polymeric material. The claims merely recite that a different polymer other than the polymeric particle be present.

Applicant argued, "With respect to claim 32, nowhere does Golomb disclose, either expressly or inherently, a device coating free from any therapeutic substances but including particles of a polymeric material having a therapeutic substance added thereto."

Applicant's arguments were not held persuasive. The secondary reference of Wang ('379) was relied upon for resolving this deficiency of Golomb by their teaching of a stent that can have multiple layers, whereby one layer can be free from any active ingredient. Thus, this teaching is sufficient to meet Applicant's claim limitation.

Applicant argued, "Claim 28 is independently patentable. Nowhere does Golomb disclose that the polymeric particles have a hydrogel consistency."

The Examiner was not persuaded by this argument. There is no showing of any unexpected results with respect to the polymeric material formed of a hydrogel material. The

polymeric particles of the art provide for the same beneficially effective results for sufficiently treating restenosis, as is desired by Applicant.

- **Rejection under 35 U.S.C. §103(a) over Golomb (U.S. Pat. No. 6,719,998) in view of Wang (U.S. Pat. No. 6,379,379):**

Applicant argued, "Wang does not remedy the deficiencies of Golomb. Wang does not disclose, either expressly or inherently, drug-containing polymeric particles embedded within a coating layer on a stent. Furthermore, even if Wang suggested a drug-containing polymeric particle, which it does not, Wang does not disclose, either expressly or inherently, that the stent coating layer would include an additional "...polymer different than the polymer from which the particles are made".

Applicant's arguments have been considered but were not persuasive. The Wang reference was relied upon to demonstrate a coating layer that does not require use of an active ingredient and thus resolves the deficiency of Golomb. Furthermore, the Golomb reference explicitly teaches compositions comprising active ingredient that is formulated in a manner to allow it's incorporation onto a stent, such as for example, by including it within a coating of the stent (col. 3, lines 55-60). The argument that "an additional polymer different than the polymer from which the particles are made" is not taught was not persuasive. As delineated above, Applicant has not established any unexpected or superior results, which accrues from the use of providing an additional polymer other than the particles from which the polymer is made. The prior art provides for a composition having essentially the same elements, being used in the same art area, to achieve the same results and treat the same problems, the Applicant providing no

showing of any unexpected result. It is the position of the Examiner that the claims remain generic enough to read on the teachings of the prior art, either alone or in combination. Thus, the rejections of record have been maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

--No claims are allowed at this time.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday during regular business hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley, can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Humera N. Sheikh/

Primary Examiner, Art Unit 1618

hns

May 21, 2008